

General

Guideline Title

Role of bone-modifying agents in metastatic breast cancer: an American Society of Clinical Oncology–Cancer Care Ontario focused guideline update.

Bibliographic Source(s)

Van Poznak C, Somerfield MR, Barlow WE, Biermann JS, Bosserman LD, Clemons MJ, Dhesy-Thind SK, Dillmon MS, Eisen A, Frank ES, Jagsi R, Jimenez R, Theriault RL, Vandenberg TA, Yee GC, Moy B. Role of bone-modifying agents in metastatic breast cancer: an American Society of Clinical Oncology–Cancer Care Ontario focused guideline update. J Clin Oncol. 2017 Dec 10;35(35):3978-86. [22 references]
[PubMed](#)

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Van Poznak CH, Temin S, Yee GC, Janjan NA, Barlow WE, Biermann JS, Bosserman LD, Geoghegan C, Hillner BE, Theriault RL, Zuckerman DS, Von Roenn JH. American Society of Clinical Oncology clinical practice guideline update on the role of bone-modifying agents in metastatic breast cancer. Alexandria (VA): American Society of Clinical Oncology (ASCO); 2011. 17 p.

This guideline meets NGC's 2013 (revised) inclusion criteria.

NEATS Assessment

National Guideline Clearinghouse (NGC) has assessed this guideline's adherence to standards of trustworthiness, derived from the Institute of Medicine's report [Clinical Practice Guidelines We Can Trust](#).

■■■■= Poor ■■■= Fair ■■■= Good ■■■= Very Good ■■■= Excellent

Assessment	Standard of Trustworthiness
YES	Disclosure of Guideline Funding Source

■■■■■	Disclosure and Management of Financial Conflict of Interests
	Guideline Development Group Composition
YES	Multidisciplinary Group
YES	Methodologist Involvement
■■■■■	Patient and Public Perspectives
	Use of a Systematic Review of Evidence
■■■■■	Search Strategy
■■■■■	Study Selection
■■■■■	Synthesis of Evidence
	Evidence Foundations for and Rating Strength of Recommendations
■■■■■	Grading the Quality or Strength of Evidence
■■■■■	Benefits and Harms of Recommendations
■■■■■	Evidence Summary Supporting Recommendations
■■■■■	Rating the Strength of Recommendations
■■■■■	Specific and Unambiguous Articulation of Recommendations
■■■■■	External Review
■■■■■	Updating

Recommendations

Major Recommendations

Definitions for the rating of evidence (High, Intermediate, Low, Insufficient); types of recommendations (Evidence based, Formal consensus, Informal consensus, No recommendation); and strength of recommendations (Strong, Moderate, Weak) are provided at the end of the "Major Recommendations" field.

Clinical Question 1

What are the best intervals between dosing of zoledronic acid?

Updated Recommendation. As recommended in the 2011 version of the American Society of Clinical Oncology (ASCO) bone-modifying agents (BMAs) guideline, patients with breast cancer who have evidence of bone metastases should be treated with BMAs. One BMA is not recommended over another. If patients are treated with zoledronic acid, 4 mg intravenously administered over no less than 15 minutes, dosing

options are every 12 weeks or every 3 to 4 weeks (Type: evidence based, benefits outweigh harms; Evidence quality: high; Strength of recommendation: strong).

Clinical Question 2

What is the role of BMAs in control of pain secondary to bone metastases?

Updated Recommendation. The analgesic effects of BMAs (denosumab, pamidronate, or zoledronic acid) are modest, and BMAs should not be used alone for bone pain. The Update Committee recommends that the current standard of care for supportive care and pain management be applied. This can include analgesia, adjunct therapies, radiotherapy, surgery, systemic anticancer therapy, and referral to supportive care and pain management. Evidence of a clinically meaningful benefit is insufficient to support the use of one BMA over another. Further research is needed on this clinical question (Type: evidence based, benefits outweigh harms; Evidence quality: low; Strength of recommendation: weak).

Refer to the "Bottom Line" page in the original guideline document for recommendations unchanged from the 2011 guideline update (see the "Availability of Companion Documents" field).

Definitions

Guide for Rating Quality of Evidence

Rating for Strength of Evidence	Definition
High	High confidence that the available evidence reflects the true magnitude and direction of the net effect (i.e., balance of benefits versus harms) and that further research is very unlikely to change either the magnitude or direction of this net effect.
Intermediate	Moderate confidence that the available evidence reflects the true magnitude and direction of the net effect. Further research is unlikely to alter the direction of the net effect; however, it might alter the magnitude of the net effect.
Low	Low confidence that the available evidence reflects the true magnitude and direction of the net effect. Further research may change either the magnitude and/or direction this net effect.
Insufficient	Evidence is insufficient to discern the true magnitude and direction of the net effect. Further research may better inform the topic. The use of the consensus opinion of experts is reasonable to inform outcomes related to the topic.

Guide for Types of Recommendations

Type of Recommendation	Definition
Evidence based	There was sufficient evidence from published studies to inform a recommendation to guide clinical practice.
Formal consensus	The available evidence was deemed insufficient to inform a recommendation to guide clinical practice. Therefore, the Expert Panel used a formal consensus process to reach this recommendation, which is considered the best current guidance for practice. The Expert Panel may choose to provide a rating for the strength of the recommendation (i.e., "strong," "moderate," or "weak"). The results of the formal consensus process are summarized in the guideline and reported in the Data Supplement (see the "Availability of Companion Documents" field).
Informal consensus	The available evidence was deemed insufficient to inform a recommendation to guide clinical practice. The recommendation is considered the best current guidance for practice, based on informal consensus of the Expert Panel. The Expert Panel agreed that a formal consensus process was not necessary for reasons described in the literature review and discussion. The Expert Panel may choose to provide a rating for the strength of the recommendation (i.e., "strong," "moderate," or "weak").
No	There is insufficient evidence, confidence, or agreement to provide a

Type of Recommendation	Definition
recommendation	recommendation to guide clinical practice at this time. The Expert Panel deemed the available evidence as insufficient and concluded it was unlikely that a formal consensus process would achieve the level of agreement needed for a recommendation.

Guide for Strength of Recommendations

Rating for Strength of Recommendation	Definition
Strong	There is high confidence that the recommendation reflects best practice. This is based on (1) strong evidence for a true net effect (e.g., benefits exceed harms); (2) consistent results, with no or minor exceptions; (3) minor or no concerns about study quality; and/or (4) the extent of Expert Panelists' agreement. Other compelling considerations (discussed in the guideline's literature review and analyses) may also warrant a strong recommendation.
Moderate	There is moderate confidence that the recommendation reflects best practice. This is based on (1) good evidence for a true net effect (e.g., benefits exceed harms); (2) consistent results, with minor and/or few exceptions; (3) minor and/or few concerns about study quality; and/or (4) the extent of Expert Panelists' agreement. Other compelling considerations (discussed in the guideline's literature review and analyses) may also warrant a moderate recommendation.
Weak	There is some confidence that the recommendation offers the best current guidance for practice. This is based on (1) limited evidence for a true net effect (e.g., benefits exceed harms); (2) consistent results, but with important exceptions; (3) concerns about study quality; and/or (4) the extent of Expert Panelists' agreement. Other considerations (discussed in the guideline's literature review and analyses) may also warrant a weak recommendation.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Metastatic breast cancer with bone metastases

Guideline Category

Assessment of Therapeutic Effectiveness

Management

Treatment

Clinical Specialty

Internal Medicine

Obstetrics and Gynecology

Oncology

Intended Users

Advanced Practice Nurses

Nurses

Patients

Pharmacists

Physician Assistants

Physicians

Guideline Objective(s)

- To update, in collaboration with Cancer Care Ontario (CCO), key recommendations of the American Society of Clinical Oncology (ASCO) guideline on the role of bone-modifying agents (BMAs) in metastatic breast cancer
- To address the new data on intervals between dosing and the role of BMAs in control of bone pain

Target Population

Patients with breast cancer with evidence of bone metastases

Interventions and Practices Considered

1. Bone-modifying agents (BMAs)
 - Denosumab
 - Pamidronate
 - Zoledronic acid
2. Supportive care and pain management (i.e., analgesia, adjunct therapies, radiotherapy, surgery, systemic anticancer therapy, and referral to supportive care and pain management)

Major Outcomes Considered

- Skeletal-related events (SREs) (fracture, radiation, surgery to bone or spinal cord compression, hypercalcemia)
- Skeletal morbidity rates (SMRs)
- Pain
- Analgesic use
- Adverse events
- Quality of life

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Guideline Update Process

The Update Committee conducted a search of the PubMed database to identify systematic reviews, meta-analyses, and randomized controlled trials (RCTs) that addressed the role of bone-modifying agents (BMAs) in the management of metastatic breast cancer. The review of the yield from this search focused on publications that reported on 4-week and 12-week intervals between the dosing of zoledronic acid and the role of BMAs in control of pain secondary to bone metastases.

The PubMed search (from January 2011 to March 2017) conducted to identify publications that reported on studies of the optimal intervals between BMA dosing and studies addressing the role of BMAs in control of pain secondary to bone metastases yielded 273 records.

To inform the special commentary on cost considerations, the Update Committee conducted an additional targeted PubMed literature search to identify articles reporting on the results of cost-effectiveness analyses of BMAs. This search was limited to non-industry-supported studies.

The PubMed literature search (2003 to July 2016) performed to identify articles reporting on the results of cost-effectiveness analyses of BMAs yielded 32 records; however, none of the publications provided new evidence to inform the special commentary on cost considerations. A bibliography of the results of the cost-effectiveness literature search is provided in Data Supplement 3 (see the "Availability of Companion Documents" field).

Details of the searches are provided in the Data Supplement 1 (see the "Availability of Companion Documents" field).

Number of Source Documents

After review of the identified abstracts, six full-text articles—three phase III noninferiority trials of dosing intervals, one systematic review and meta-analysis of studies of de-escalation of bone-modifying agents (BMAs), and two randomized controlled trials (RCTs) of the role of BMAs in control of pain secondary to bone metastases—were selected for review by the Update Committee.

See Data Supplement 2 (see the "Availability of Companion Documents" field) for Quality of Reporting of Meta-analyses (QUOROM) Diagrams showing exclusions and inclusions of publications identified for the systematic review.

Methods Used to Assess the Quality and Strength of the Evidence

Expert Consensus

Rating Scheme for the Strength of the Evidence

Guide for Rating Quality of Evidence

Rating for Strength of Evidence	Definition
High	High confidence that the available evidence reflects the true magnitude and direction of the net effect (i.e., balance of benefits versus harms) and that further research is very unlikely to change either the magnitude or direction of this net effect.
Intermediate	Moderate confidence that the available evidence reflects the true magnitude and direction of the net effect. Further research is unlikely to alter the direction of the net effect; however, it might alter the magnitude of the net effect.
Low	Low confidence that the available evidence reflects the true magnitude and direction of the net effect. Further research may change either the magnitude and/or direction this net effect.

Rating for Strength of Evidence	Definition
	Evidence is insufficient to discern the true magnitude and direction of the net effect. Further research may better inform the topic. The use of the consensus opinion of experts is reasonable to inform outcomes related to the topic.

Guide for Rating of Potential for Bias

Rating of Potential for Bias	Definitions for Rating Potential for Risk of Bias in Randomized Controlled Trials
Low risk	No major features in the study that risk biased results, and none of the limitations are thought to decrease the validity of the conclusions. The study avoids problems such as failure to apply true randomization, selection of a population unrepresentative of the target patients, high dropout rates, and no intention-to-treat analysis; and key study features are described clearly (including the population, setting, interventions, comparison groups, measurement of outcomes, and reasons for dropouts).
Intermediate	The study is susceptible to some bias, but flaws are not sufficient to invalidate the results. Enough of the items introduce some uncertainty about the validity of the conclusions. The study does not meet all the criteria required for a rating of good quality, but no flaw is likely to cause major bias. The study may be missing information, making it difficult to assess limitations and potential problems.
High risk	There are significant flaws that imply biases of various types that may invalidate the results. Several of the items introduce serious uncertainty about the validity of the conclusions. The study has serious errors in design, analysis, or reporting; large amounts of missing information; or discrepancies in reporting.

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Not stated

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Panel Composition

The American Society of Clinical Oncology (ASCO) Clinical Practice Guidelines Committee (CPGC) and the ASCO Breast Cancer Guideline Advisory Group (GAG) convened an Update Committee with multidisciplinary representation in medical oncology, radiation oncology, surgical oncology, and community oncology. The panel included a member of Practice Guidelines Implementation Network, and patient/advocacy representation. The Expert Panel was led by two Co-Chairs who had the primary responsibility for the development and timely completion of the guideline. The Panel had one face-to-face meeting. The Co-Chairs and ASCO staff prepared a draft guideline for review and rating by the Expert Panel.

For this joint ASCO-Cancer Care Ontario (CCO) focused guideline update, CCO appointed formal representatives.

Guideline Update Process

The American Society of Clinical Oncology (ASCO) uses a signals approach to facilitate guideline updating. This approach identifies new, potentially practice-changing data—signals—that might translate into revised practice recommendations. The approach relies on targeted literature searching and the expertise of ASCO guideline panel members to identify signals.

For this focused update, a set of three phase III randomized noninferiority trials addressing dosing interval of zoledronic acid provided the signal. Primarily on the basis of this signal, the ASCO Breast Cancer Advisory Group ranked updating the guideline on bone-modifying agents (BMAs) in metastatic breast cancer among its highest priorities. To that end, ASCO and CCO convened a joint Update Committee to review the evidence and to formulate updated recommendations for practice. With the approval of the ASCO Breast Cancer Guideline Advisory Group, the Update Committee expanded the guideline scope to include a commentary on cost considerations in the use of BMAs in patients with metastatic breast cancer.

The entire Update Committee contributed to the development of the guideline, provided critical review, and finalized the guideline recommendations.

Guideline Development Process

The full Update Committee met once and corresponded frequently through email; progress on guideline development was driven primarily by the Co-Chairs and ASCO staff. The purpose of the Panel meetings was for members to contribute content, provide critical review, interpret evidence, and finalize the guideline recommendations based upon the consideration of the evidence.

Development of Recommendations

The guideline recommendations were rated, in part, using the principles of the GuideLines Into DEcision Support (GLIDES) methodology.

Rating Scheme for the Strength of the Recommendations

Guide for Types of Recommendations

Type of Recommendation	Definition
Evidence based	There was sufficient evidence from published studies to inform a recommendation to guide clinical practice.
Formal consensus	The available evidence was deemed insufficient to inform a recommendation to guide clinical practice. Therefore, the Expert Panel used a formal consensus process to reach this recommendation, which is considered the best current guidance for practice. The Expert Panel may choose to provide a rating for the strength of the recommendation (i.e., "strong," "moderate," or "weak"). The results of the formal consensus process are summarized in the guideline and reported in the Data Supplement (see the "Availability of Companion Documents" field).
Informal consensus	The available evidence was deemed insufficient to inform a recommendation to guide clinical practice. The recommendation is considered the best current guidance for practice, based on informal consensus of the Expert Panel. The Expert Panel agreed that a formal consensus process was not necessary for reasons described in the literature review and discussion. The Expert Panel may choose to provide a rating for the strength of the recommendation (i.e., "strong," "moderate," or "weak").
No recommendation	There is insufficient evidence, confidence, or agreement to provide a recommendation to guide clinical practice at this time. The Expert Panel deemed the available evidence as insufficient and concluded it was unlikely that a formal consensus process would achieve the level of agreement needed for a recommendation.

Rating for Strength of Recommendation	Definition
Strong	There is high confidence that the recommendation reflects best practice. This is based on (1) strong evidence for a true net effect (e.g., benefits exceed harms); (2) consistent results, with no or minor exceptions; (3) minor or no concerns about study quality; and/or (4) the extent of Expert Panelists' agreement. Other compelling considerations (discussed in the guideline's literature review and analyses) may also warrant a strong recommendation.
Moderate	There is moderate confidence that the recommendation reflects best practice. This is based on (1) good evidence for a true net effect (e.g., benefits exceed harms); (2) consistent results, with minor and/or few exceptions; (3) minor and/or few concerns about study quality; and/or (4) the extent of Expert Panelists' agreement. Other compelling considerations (discussed in the guideline's literature review and analyses) may also warrant a moderate recommendation.
Weak	There is some confidence that the recommendation offers the best current guidance for practice. This is based on (1) limited evidence for a true net effect (e.g., benefits exceed harms); (2) consistent results, but with important exceptions; (3) concerns about study quality; and/or (4) the extent of Expert Panelists' agreement. Other considerations (discussed in the guideline's literature review and analyses) may also warrant a weak recommendation.

Cost Analysis

The search for published cost-effectiveness analyses that might inform the clinical question of the relative value of available BMAs provided no definitive evidence to inform cost considerations. The Update Committee excluded articles from consideration identified from a first-level review of the literature search (see the Data Supplement [see the "Availability of Companion Documents" field]) because the analyses in question lacked contemporary cost data for the agents studied, included agents that are not currently available in either the United States or Canada, and/or were industry sponsored.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

The American Society of Clinical Oncology (ASCO) Clinical Practice Guidelines Committee (CPCG) reviews and approves all ASCO guidelines. In addition, the Cancer Care Ontario Report Approval Panel reviewed this focused update manuscript.

The draft guideline document was disseminated for external review and submitted to the *Journal of Clinical Oncology (JCO)* for peer review and publication.

The ASCO CPCG approved this guideline on June 25, 2017.

The Cancer Care Ontario Report Approval Panel approved this guideline on July 26, 2017.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

When used concurrently with analgesics, bone-modifying agents (BMAs) may be of benefit for women with metastatic breast cancer with pain caused by bone metastases.

Refer to the "Literature review update and analysis" section of the original guideline document for a detailed discussion of the potential benefits of each recommendation.

Potential Harms

- Renal adverse events and osteonecrosis of the jaw (ONJ) are adverse events related to zoledronic acid.
- In three randomized controlled trials (RCTs), the comparisons between dosing the bone-modifying agents (BMAs) every 4 weeks or every 12 weeks showed a similar rate of skeletal complications as measured by proportion of skeletal-related events (SREs) or skeletal morbidity rates (SMRs) between the 4-week and 12-week dosing study arms. SREs are defined as fracture, radiation, or surgery to bone or spinal cord compression. One of the studies also included hypercalcemia as an SRE. SMR is defined as the number of SREs over time.
- In one study, the most common treatment-emergent adverse event related to zoledronic acid was a rise in serum creatinine leading to discontinuation of the study drug.

Refer to the "Literature review update and analysis" section of the original guideline document for a detailed discussion of the potential harms of each recommendation.

Qualifying Statements

Qualifying Statements

- The Clinical Practice Guidelines and other guidance published herein are provided by the American Society of Clinical Oncology, Inc. (ASCO) to assist providers in clinical decision making. The information herein should not be relied upon as being complete or accurate, nor should it be considered as inclusive of all proper treatments or methods of care or as a statement of the standard of care. With the rapid development of scientific knowledge, new evidence may emerge between the time information is developed and when it is published or read. The information is not continually updated and may not reflect the most recent evidence. The information addresses only the topics specifically identified therein and is not applicable to other interventions, diseases, or stages of diseases. This information does not mandate any particular course of medical care. Further, the information is not intended to substitute for the independent professional judgment of the treating provider, as the information does not account for individual variation among patients. Recommendations reflect high, moderate, or low confidence that the recommendation reflects the net effect of a given course of action. The use of words like "must," "must not," "should," and "should not" indicates that a course of action is recommended or not recommended for either most or many patients, but there is latitude for the treating physician to select other courses of action in individual cases. In all cases, the selected course of See the "Health Disparities" section in the

original guideline document for additional qualifying information. action should be considered by the treating provider in the context of treating the individual patient. Use of the information is voluntary. ASCO provides this information on an "as is" basis and makes no warranty, express or implied, regarding the information. ASCO specifically disclaims any warranties of merchantability or fitness for a particular use or purpose. ASCO assumes no responsibility for any injury or damage to persons or property arising out of or related to any use of this information, or for any errors or omissions.

- Cancer Care Ontario's Program in Evidence-Based Care, the cancer guidelines initiative of the Ontario cancer system, supports and endorses these disclaimer principles.

Implementation of the Guideline

Description of Implementation Strategy

For information on the American Society for Clinical Oncology (ASCO) implementation strategy, see the [ASCO Web site](#) .

Implementation Tools

Patient Resources

Quick Reference Guides/Physician Guides

Slide Presentation

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Safety

Identifying Information and Availability

Bibliographic Source(s)

Van Poznak C, Somerfield MR, Barlow WE, Biermann JS, Bosserman LD, Clemons MJ, Dhesy-Thind SK,

Dillmon MS, Eisen A, Frank ES, Jagsi R, Jimenez R, Theriault RL, Vandenberg TA, Yee GC, Moy B. Role of bone-modifying agents in metastatic breast cancer: an American Society of Clinical Oncology-Cancer Care Ontario focused guideline update. J Clin Oncol. 2017 Dec 10;35(35):3978-86. [22 references] [PubMed](#)

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2017 Dec

Guideline Developer(s)

American Society of Clinical Oncology - Medical Specialty Society

Source(s) of Funding

American Society of Clinical Oncology (ASCO)

Guideline Committee

Role of Bone-Modifying Agents in Metastatic Breast Cancer: American Society of Clinical Oncology and Cancer Care Ontario Update Expert Panel

Composition of Group That Authored the Guideline

Expert Panel Members: Beverly Moy, MD (*Co-chair*), Massachusetts General Hospital, Boston, MA; Catherine Van Poznak, MD (*Co-chair*), University of Michigan, Ann Arbor, MI; William E. Barlow, PhD, Cancer Research and Biostatistics, Seattle, WA; J. Sybil Biermann, MD, University of Michigan, Ann Arbor, MI; Linda D. Bosserman, MD, City of Hope, Duarte, CA; Mark J. Clemons, MD, The Ottawa Hospital Cancer Centre, Ottawa, Canada; Sukhbinder K. Dhesy-Thind, MD, Juravinski Cancer Centre, Hamilton, Canada; Melissa S. Dillmon, MD, Practice Guideline Implementation Network (PGIN), Harbin Clinic, Rome, GA; Andrea Eisen, MD, Odette Cancer Centre, Toronto, ON, Canada; Elizabeth S. Frank, Dana-Farber Cancer Institute, Boston, MA; Reshma Jagsi, MD, University of Michigan Comprehensive Cancer Center, Ann Arbor, MI; Rachel Jimenez, MD, Massachusetts General Hospital, Boston, MA; Richard L. Theriault, DO, MD, Anderson Cancer Center, Houston, TX; Theodore A. Vandenberg, MD, London Regional Cancer Program, London, ON, Canada; Gary C. Yee, PharmD, University of Nebraska Medical Center, Omaha, NE; Mark R. Somerfield, PhD (*American Society of Clinical Oncology staff*)

Financial Disclosures/Conflicts of Interest

Guideline and Conflicts of Interest

The Expert Panel was assembled in accordance with the American Society of Clinical Oncology's (ASCO's) Conflict of Interest Management Procedures for Clinical Practice Guidelines ("Procedures," summarized at <https://www.asco.org/about-asco/legal/conflict-interest>). Members of the Panel completed ASCO's disclosure form, which requires disclosure of financial and other interests that are relevant to the subject matter of the guideline, including relationships with commercial entities that are reasonably likely to experience direct regulatory or commercial effect as a result of promulgation of the

guideline. Categories for disclosure include employment; leadership; stock or other ownership; honoraria, consulting or advisory role; speaker's bureau; research funding; patents, royalties, other intellectual property; expert testimony; travel, accommodations, expenses; and other relationships. In accordance with the Procedures, the majority of the members of the Panel did not disclose any such relationships.

Authors' Disclosures and Potential Conflicts of Interest

The following represents disclosure information provided by authors of the guideline. All relationships are considered compensated. Relationships are self-held unless noted. I = Immediate Family Member, Inst = My Institution. Relationships may not relate to the subject matter of this manuscript. For more information about ASCO's conflict of interest policy, please refer to <https://www.asco.org/about-asco/legal/conflict-interest> or ascopubs.org/jco/site/ifc .

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Research Funding: Bayer (Inst)

Patents, Royalties, Other Intellectual Property: UpToDate

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No relationship to disclose

William Barlow

Research Funding: AstraZeneca (Inst), Merck (Inst)

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No relationship to disclose

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Leadership: Anthem Blue Cross Wellpoint, LA County Fair

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Association of Nurse Navigators, Medscape, Physicians Education Resource, JADPRO, AstraZeneca

Consulting or Advisory Role: Pfizer, ACCC, Novartis, Sandoz-Novartis, Merck, Puma Biotechnology

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No relationship to disclose

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Honoraria: Pharmacy Times

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Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Van Poznak CH, Temin S, Yee GC, Janjan NA, Barlow WE, Biermann JS, Bosserman LD, Geoghegan C, Hillner BE, Theriault RL, Zuckerman DS, Von Roenn JH. American Society of Clinical Oncology clinical practice guideline update on the role of bone-modifying agents in metastatic breast cancer. Alexandria (VA): American Society of Clinical Oncology (ASCO); 2011. 17 p.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available from the [Journal of Clinical Oncology Web site](#) .

Availability of Companion Documents

The following are available:

Role of bone-modifying agents in metastatic breast cancer: an American Society of Clinical Oncology–Cancer Care Ontario focused guideline update. Data supplement. Alexandria (VA): American Society of Clinical Oncology; 2017. 13 p. Available from the [Journal of Clinical Oncology Web site](#) .

Role of bone-modifying agents in metastatic breast cancer: an American Society of Clinical Oncology–Cancer Care Ontario focused guideline update. Methods supplement. Alexandria (VA): American Society of Clinical Oncology; 2017. 6 p. Available from the [Journal of Clinical Oncology Web site](#) .

Role of bone-modifying agents in metastatic breast cancer: an American Society of Clinical Oncology–Cancer Care Ontario focused guideline update summary. J Oncol Pract. 2017 Dec;13(12):822-4. Available to subscribers from the [Journal of Oncology Practice Web site](#) .

Role of bone-modifying agents in metastatic breast cancer: an American Society of Clinical Oncology–Cancer Care Ontario focused guideline update. Summary of recommendations table. Alexandria (VA): American Society of Clinical Oncology; 2017. 2 p. Available from the [American Society of Clinical Oncology \(ASCO\) Web site](#) .

Role of bone-modifying agents in metastatic breast cancer: an American Society of Clinical Oncology–Cancer Care Ontario focused guideline update. Slide set. Alexandria (VA): American Society of Clinical Oncology; 2017. 14 p. Available in [PDF](#) and [PowerPoint](#) from the ASCO Web site.

Van Poznak CH, Temin S, Yee GC, Janjan NA, Barlow WE, Biermann JS, Bosserman LD, Geoghegan C, Hillner BE, Theriault RL, Zuckerman DS, Von Roenn JH. American Society of Clinical Oncology executive summary of the clinical practice guideline update on the role of bone-modifying agents in metastatic breast cancer. J Clin Oncol 2011 Mar 20;29(9):1221-7. Available from the [Journal of](#)

Patient Resources

The following is available:

Breast cancer - metastatic. Patient information. [internet]. Alexandria (VA): American Society of Clinical Oncology (ASCO); 2017 Apr. Available from the [Cancer.Net Web site](#)

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

This NGC summary was completed by ECRI on September 21, 2000. The guideline developer was provided with a copy of this NGC summary for review, but to date, NGC has not received any comments from the guideline developer. This guideline was updated by ECRI on February 16, 2004. The updated information was verified by the guideline developer on February 26, 2004. This summary was updated by ECRI on March 28, 2005, following the U.S. Food and Drug Administration advisory on Zometa (zoledronic acid). This summary was updated on May 3, 2005 following the withdrawal of Bextra (valdecoxib) from the market and the release of heightened warnings for Celebrex (celecoxib) and other nonselective nonsteroidal anti-inflammatory drugs (NSAIDs). This summary was updated by ECRI on May 20, 2005, following the U.S. Food and Drug Administration advisory on Aredia (pamidronate disodium) and Zometa (zoledronic acid). This summary was updated by ECRI on June 16, 2005, following the U.S. Food and Drug Administration advisory on COX-2 selective and non-selective non-steroidal anti-inflammatory drugs (NSAIDs). This summary was updated by ECRI Institute on June 15, 2011. This summary was updated by ECRI Institute on September 18, 2015 following the U.S. Food and Drug Administration advisory on non-aspirin nonsteroidal anti-inflammatory drugs (NSAIDs). This summary was updated by ECRI Institute on June 2, 2016 following the U.S. Food and Drug Administration advisory on opioid pain medicines. This summary was updated by ECRI Institute on October 21, 2016 following the U.S. Food and Drug Administration advisory on opioid pain and cough medicines combined with benzodiazepines. This summary was completed by ECRI Institute on March 15, 2018. The guideline developer agreed to not review the content.

This NEATS assessment was completed by ECRI Institute on February 1, 2018. The guideline developer agreed to not review the content.

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